CLAIMS

1. A stabilized pharmaceutical solid composition of ACE inhibitor comprising an ACE inhibitor and a selective dosage formulation thereof comprising of meglumine.

2. A composition of claim 1, where in the ACE inhibitor is selected from the group of enalapril, delapril, lisinopril, moxipril, perindopril, ramipril, trandolapril and pharmaceutically acceptable salts thereof.

3. A composition of claim 2, wherein the ACE-inhibitor is ramipril.

4. A composition of claim 3, wherein the amount of ramipril in the composition is from about 1.25 mg to about 10 mg.

5. A composition of anyone of claims 1 to 4 , wherein the ratio of ACE-inhibitor to meglumine is from about 1:0.01 to about 1:2.0.

6. A composition of claim 5 , wherein the ratio of ACE-inhibitor to meglumine is preferably from about 1:0.03 to about 1:1.2.

7. A composition of anyone of claims 1 to 6 wherein the dosage formulation further contains a diluent.

8. A composition of claim 7, wherein the diluent is selected from amongst low substituted hydroxypropyl cellulose or pregelatinized starch.

9. A composition of anyone of claims 1 to 7, wherein the ratio of ACE-inhibitor to diluent is from about 1:10 to about 1:100.

10. A composition of anyone of claims 1 to 10 wherein the dosage formulation further contains lubricant.

11. A composition of claim 11, wherein the lubricant is a stearate, which is selected from the group consisting of magnesium stearate, zinc stearate and calcium stearate.

12. A composition of claim 12,wherein the lubricant is magnesium stearate.

13. A composition of anyone of claims 1 to 13, wherein the amount of lubricant in the composition is from about 0.2 mg to about 2 mg.

14. A composition of claim 14, wherein the amount of lubricant in the composition is preferably from about 0.5 mg to about 1.5 mg.

15. A stabilized pharmaceutical ACE inhibitor composition comprising ramipril and a dosage formulation comprising of meglumine along with atleast one of low substituted hydroxypropyl cellulose and pregelatinized starch and magnesium stearate.

16. A composition of anyone of claims 1 to 16 in any dosage form preferably is filled into a capsule or compressed to a tablet.

17. The process for the preparation of a stable formulation of ACE-inhibitor comprising mixing of the ACE inhibitor with a selective dosage formulation comprising of meglumine and a diluent followed by compressing the mixture to a tablet or filling it into a capsule.

18. The process as claimed in claim 18 wherein the diluent is selected from amongst low substituted hydroxypropyl cellulose and pregelatinized starch.

19. A stabilized pharmaceutical solid composition of ACE inhibitor and its process for manufacture substantially as described and exemplified herein.

AMENDED CLAIMS
[received by the International Bureau on 1st November 2004 (01.11.04);
original claims 1-19 replaced by amended claims 1-23 (2pages).]

+statement

1. A stabilized pharmaceutical solid composition comprising of an ACE inhibitor and meglumine.

2. A stabilized composition of claim 1, where in the ACE inhibitor is selected from the group of enalapril, delapril, lisinopril, moxipril, perindopril, ramipril, trandolapril and pharmaceutically acceptable salts thereof.

3. A stabilized composition of claim 2, wherein the ACE-inhibitor is ramipril.

4. A stabilized composition of claim 3, wherein the amount of ramipril in the composition is from about 1 mg to about 10 mg.

5. A stabilized composition of claim 1, wherein the ratio of ACE-inhibitor to meglumine is from about 1:0.01 to about 1:2.0.

6. A stabilized composition of claim 5, wherein the ratio of ACE-inhibitor to meglumine is preferably from about 1:0.03 to about 1:1.2.

7. A stabilized composition of claim 1, which further comprises of a diluent.

8. A stabilized composition of claim 7, wherein the diluent is selected from amongst low substituted hydroxypropyl cellulose and pregelatinized starch.

9. A stabilized composition of claim 7, wherein the ratio of ACE-inhibitor to diluent is from about 1:10 to about 1:100.

10. A stabilized composition of claim 1 wherein the dosage formulation further comprises of lubricant.

11. A stabilized composition of claim 10, wherein the lubricant is a stearate, which is selected from the group consisting of magnesium stearate, zinc stearate and calcium stearate.

12. A stabilized composition of claim 10,wherein the lubricant is magnesium stearate.

13. A stabilized composition of claim 10, wherein the amount of lubricant in the composition is from about 0.2 mg to about 2 mg.

14. A stabilized composition of claim 10, wherein the amount of lubricant in the composition is from about 0.5 mg to about 1.5 mg.

15. A stabilized pharmaceutical ACE inhibitor composition comprising ramipril and meglumine along with atleast one of low substituted hydroxypropyl cellulose, pregelatinized starch and magnesium stearate.

16. A stabilized composition of claim 1 in any dosage form.

17. A stabilized composition of claim 16 wherein the composition is filled into a capsule.

18. A stabilized composition of claim 16 wherein the composition is made into a tablet.

19. A process of preparation of a stable formulation of ACE-inhibitor comprising mixing of the ACE inhibitor with meglumine and optionally atleast one of a diluent and a lubricant followed by compressing the mixture to a tablet or filling the mixture into a capsule.

20. The process as claimed in Claim 19 wherein the diluent is selected from amongst low substituted hydroxypropyl cellulose and pregelatinized starch.

21. The process as claimed in Claim 19 wherein the lubricant, is selected from the group consisting of magnesium stearate, zinc stearate and calcium stearate.

22. The process as claimed in Claim 21 wherein the lubricant is magnesium stearate.

23. A stabilized pharmaceutical solid composition of ACE inhibitor and its process for manufacture substantially as described and exemplified herein.

STATEMENT UNDER ARTICLE 19(1) RULE 46.4

WO 03/063825 cited in the International Search Report relates to a pharmaceutical composition directed to alleviate the problems of extended release profile of therapeutically active composition with limited solubility in aqueous or biological fluids. Further the cited art is directed to achieving the delivery of the therapeutically active ingredient from the composition such that it is not affected by the intrinsic solubility of the active and the released property of the solubility modifying agent. The said composition comprises a tablet core of the therapeutically active ingredient, solubility modifier, osmagents and other conventional excipients. The therapeutic active ingredient of the invention is weakly acidic in nature and is having a limited solubility in the aqueous environment. The tablet core is coated with a rate controlling semi-permeable and permeable membrane forming polymers. The solubility modifiers are in immediate contact with the active ingredient and are capable of improving the solubility of the agent by elevating the microenviromental pH above the pKa of the therapeutically active ingredient and thus improve its release profile from the pharmaceutical composition. Due to this, the release of the therapeutically active ingredient from the composition will be independent of its intrinsic water solubility and the environment of use.

There are many solubility modifiers mentioned in the cited art which are alkalinizing agents and /or buffers and Meglumine has been mentioned as one of the solubility modifiers. Among various therapeutically active ingredients cardiovascular agents are mentioned as one of the therapeutically active ingredients in which ACE inhibitors are covered under the category of cardiovascular drugs. Amongst the ACE inhibitors, only captopril is mentioned. The ratio of the therapeutically active ingredient to alkalinizing agent is in the range of 0.1: 9.9 to 7.3.

On the other hand the present invention relates to a composition comprising ACE inhibitor and Meglumine. It is directed to achieving stabilization of ACE inhibitor in a composition for increased shelf life by incorporation of meglumine. The inventors have found that the degradation of the ACE inhibitors on contact with some pharmaceutical excipients can be prevented by use of meglumine. The incorporation of meglumine avoids the degradation of the ACE inhibitor due to cyclization via the internal nucleophilic attack to form substituted diketopiperazines, hydrolysis of the side chain ester group and oxidation to form products having often unwanted coloration. Accordingly such composition comprising ACE inhibitors and meglumine are stable and have long shelf life.

Though WO 03/063825 indicates meglumine as one of the solubility modifiers/alkalinizing agent and captopril as one of the cardiovascular agent but not ACE inhibitor specifically, it does not teach or suggest a composition essentially comprising ACE inhibitor and meglumine such that meglumine would avoid the degradation of the ACE as above. Moreover the ratio in which the active and alkanizing agent are combined is different from that in which the ACE inhibitor and meglumine is present in the composition of the present invention.

The claims are amended to further clarify the scope of protection and the same may be taken as amendment under Article 19.